

B, -- Different techniques have already been proposed to quantitatively determine the absorption and reduced scattering coefficients of turbid media. See Welch, A.J.; van Gemert, M.J.C., Optical Thermal Response of Laser Irradiated Tissue; Plenum Publishing Corp., New York, 1995, and references therein. Most of the non-invasive methods are based on the measurement of spatially and/or temporally-resolved reflectance. The principle is as follows: the turbid medium is illuminated by a collimated or focused light source. The backscattered light is measured by one or several detectors. Different types of measurements are possible, depending on the time-dependence of the illuminating source: steady-state (continuous source), time-domain (short pulsed source) or frequency domain (amplitude modulated source). The present invention relates to the case of steady-state measurements, performed at different distances  $\rho$  between the source and the detectors. However, the technique presented here can be complemented by time- or frequency-domain measurements.--

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Please replace the paragraph beginning on page 2, line 12 with the following rewritten paragraph:

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B<sub>2</sub> --1) The first case corresponds to source-detector separations larger than several transport mean free paths. For typical biological tissue optical properties (W.-F. Cheong, S.A. Prahl, and A.J. Welch, "A Review of the Optical Properties of Biological Tissues," IEEE J. Quantum Electron. 26, 2166-2185 (1990)), this case corresponds to a source-detector separation larger than 2 mm. An analytical form of the reflectance can be obtained from the diffusion equation, if the absorption coefficient  $\mu_a$  is sufficiently lower than the scattering coefficient  $\mu_s$  (typically ten times). In such a case, the relevant optical

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properties are the refractive index, the absorption coefficient and the reduced scattering coefficient. The average depth of probing is on the same order as the source-detector separation  $\rho$ .--

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Please replace the paragraph beginning on page 8, line 7 with the following rewritten paragraph:

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B<sub>3</sub>  
--The present definitions are given for clarity of the concepts developed in the patent and are worded in agreement with Welch, A.J.; van Gemert, M.J.C., Optical Thermal Response of Laser Irradiated Tissue; Plenum Publishing Corp., New York, 1995, and references therein.--

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Please replace the paragraph beginning on page 11, line 5 with the following rewritten paragraph:

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B<sub>4</sub>  
--The methods described in US Patent 5,517,987 (Tsuchiya) are based on measurements with a large range of source-detector separations, typically from 1 mfp' to 10 mfp'. In such cases, the volume probed is on the order of 10-1000 (mfp'). In contrast with such a large scale investigation, the present invention is directed to a novel approach where the volume probed is much smaller, on the order of 1 (mfp'). This is achieved by using only small source detector separations, typically from 0.1 to 2 mfp'. The lateral dimension of probing is limited to this range of distances.--

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Please replace the paragraph beginning on page 12, line 5 with the following rewritten paragraph:

58 S -- This is also one result of this simulation to compute the average depth of probing, illustrated in Fig.2. It is demonstrated that only the superficial part of the turbid medium is probed if small source-detector separations are used. For this, we determined the depth below the surface of each scattering event in the simulation. With this information we determined the average depth of all the scattering events for each detected photon, which we present as a probability density function in Fig.2. This figure shows that the average depth of scattering is approximately around 1 mfp'. Moreover it showed that the part located below 2 mfp' was not playing a significant role in the measured signal (for  $\rho < 1.5$  mfp').--

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Please replace the paragraph beginning on page 13, line 4 with the following rewritten paragraph:

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56 --Fig.3 illustrates the fact that the parameter  $\gamma$  is the only predominant parameter of the phase function that must be taken into account (and not  $g=g_1$  as frequently mentioned in literature). Different reflectance curves, obtained from Monte Carlo simulations are shown in Fig.3. Four different phase functions were used for the simulations. Three phase functions are characterized by  $\gamma=1.25$ , but different  $g_1$  and  $g_2$  values. Fig. 3 shows that almost identical reflectance curves are obtained for distances  $\rho\mu_s' > 0.3$ , if the  $g_1$  and  $g_2$  are varied in such a way that the parameter  $\gamma$  stays constant ( $\gamma=1.25$ ). For comparison, the reflectance computed with a different  $g$  ( $=g_1$ ) value is also presented ( $\gamma=2.25$ ). It appears then clearly that the parameter  $g$  ( $=g_1$ ) plays a significant role in the reflectance.--

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Please replace the paragraph beginning on page 15, line 2 with the following  
rewritten paragraph:

B7  
--In the first embodiment, the apparatus can be divided in three parts, described in  
Fig.5a.--

Please replace the paragraph beginning on page 15, line 3 with the following  
rewritten paragraph:

B8  
--The first part is the illuminating system. Any light source can be used. For  
example: a) white sources, such as halogen or xenon lights, metal halides or fluorescent  
or phosphorescent sources; b) sources such as lasers, laser diodes, optical fiber lasers,  
light emitting diodes or superluminescent diodes; c) the sources described in points a)  
and b) where monochromators, filters or interference filters are added to select a given set  
of wavelengths.--

Please replace the paragraph beginning on page 15, line 9 with the following  
rewritten paragraph:

B9  
--In the first preferred embodiment, the light power is conducted to the  
investigated sample by the probe, which is the second part of the apparatus. The probe is  
preferably made of optical fibers, to illuminate and to collect the backscattered light. But  
GRIN rods or other types of light pipes can also be used. Different possible arrangements  
of optical fibers are illustrated in Fig.6. Two different modes of measurements can be  
chosen. First, one fiber is used to illuminate the sample and at least two other fibers are  
used to collect the backscattered light at two different distances. Second, one fiber is used

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to collect the light and at least two other fibers, located at two different distances from the first one, are used to illuminate sequentially the sample.--

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Please replace the paragraph beginning on page 16, line 1 with the following rewritten paragraph:

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B, 0  
--The light collected by the probe is analyzed by the detection unit, which is the third part of the apparatus. If wide spectral light sources are used (such as halogen or xenon lights), a spectrograph can be put between the probe and the detector to get wavelength dependence of the backscattered signal (either in the source or detection unit). Any type of detector can be used. For example, photodiodes, avalanche photodiodes or photomultipliers can be assigned to each collecting fiber. Simultaneous detection of each collecting fiber can also be achieved using linear or two-dimensional detectors such as Charge-Coupled Detectors (1D or 2D), intensified CCD or array of photodiodes.--

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Please replace the paragraph beginning on page 16, line 16 with the following rewritten paragraph:

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B, 1)  
-- A second type of embodiment is presented in Fig. 5c. The difference with embodiments presented in Fig. 5a and Fig. 5b is that optionally no optical fibers, light pipes or grin rods are used. The light source unit is directly in contact with the turbid medium, as well as the detector unit. Collimating optics, micro-optics or imaging optics (DOE Diffractive Optical Elements for example) can be put between the turbid medium and the actual light sources and detectors. The different type of sources and detectors

B.11  
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cited in example for the first embodiment can be used for the second type of  
embodiments. Hybrid design, such as arrangements involving both direct contact sensors  
or detectors and fibers, light pipes or grin rods are also included in the present  
embodiment.--

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Please replace the paragraph beginning on page 17, line 5 with the following  
rewritten paragraph:

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B.12  
-- The third embodiment is described in Fig.5d and Fig.5e. The only difference  
with the first and second embodiment is that non-contact measurements are performed. A  
collimating system allows for a point-like illumination on the turbid medium. An imaging  
system enables the measurement of the spatial distribution of the reflectance. The  
detectors can be either an array (1D or 2D) of detectors (Fig.5d) with optional scanning 1  
and 2 which can operate separately or can be confounded in a single scanner, or a single  
detector (Fig.5e). In this last case, an scanning device is used to obtain the spatially-  
resolved reflectance. A fiber bundle, multicore fiber or relay optics (grin rod or multiple  
lenses) can be put between the focal point of the imaging system and the detector(s). The  
different type of sources and detectors cited in example for the first embodiment can be  
used for the third embodiment.--

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Please replace the paragraph beginning on page 17, line 16 with the following  
rewritten paragraph:

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B.13  
-- Spatial images of the parameters  $\mu_a$ ,  $\mu_s'$  and  $\gamma$  can be obtained by a series of  
measurements at different locations, that we call multi-site measurements. Some

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mechanical or optical scanning device can be used for this purpose. The resolution of such images is on the order of the mean source-detector separation used for a single site measurement. All three embodiments can be expanded to perform multi-site measurements, by duplicating and/or multiplexing the illuminating or measuring devices. For example, the optical fiber probes shown in Fig.6, can be duplicated and put side by side. The scanning system described in the third embodiment can also be expanded to perform multi-site measurements.--

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Please replace the paragraph beginning on page 19, line 4 with the following rewritten paragraph:

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B14

-- An example of a measurement, after calibration, is shown in Fig.7. The measurement was performed with the apparatus described in the first embodiment, with a probe similar to the one described in Fig.6a. A prior calibration was performed on a solid turbid medium, which optical properties were measured by another technique (frequency domain measurement, cf. Welch, A.J.; van Gemert, M.J.C., Optical Thermal Response of Laser Irradiated Tissue; Plenum Publishing Corp., New York, 1995, and references therein). The sample was a water suspension of polystyrene microsphere of 1  $\mu$ m diameter. The measurement is compared to a Monte Carlo simulation performed with the scattering properties calculated from Mie theory and absorption coefficient of water. Fig.7 shows an excellent agreement between the measurement and the simulation, which confirm the validity of our simulation model, experimental measurement and calibration.-

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Please replace the paragraph beginning on page 19, line 16 with the following rewritten paragraph:

B15 -- Artifacts during a measurement, for example due to bad contact between the probe and the sample, or heterogeneity of the sample, can be detected by the following optional procedure. Two illuminating fibers are disposed symmetrically in regard to the collecting fibers (see Fig.6b). If the sample is homogeneous, the reflectance curve should be identical with either illuminating fiber. Therefore, heterogeneity of the investigated region or obstructions beneath the fibers are detected by comparing the two curves. If the two curves are sufficiently close, the measurement is validated and the average of the two curves is calculated.--

#### IN THE CLAIMS

Please replace claim 5 with the following rewritten claim:

B16 5. (Twice Amended) The method according to claim 2, wherein the probe is put into contact with the turbid medium.

Please add the following new claims 21-41:

B17 --21. The method according to claim 4, wherein the optical and electrical micro-system is put into contact with the turbid medium.